

Appln. No. 09/155,676
Amdt. dated December 14, 2005
Reply to Office action of June 14, 2005

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-12 (Cancelled)

13 (Previously Presented). A vector comprising a DNA sequence according to claim 55.

14 (Original). A vector according to claim 13 capable of being expressed in a eukaryotic host cell.

15 (Original). A vector according to claim 13 capable of being expressed in a prokaryotic host cell.

16 (Previously Presented). Transformed eukaryotic or prokaryotic host cells containing a vector according to claim 13.

17-19 (Cancelled)

20 (Currently Amended). A An isolated NIK polypeptide according to claim 53, wherein said polypeptide is the polypeptide encoded by the nucleotide sequence of SEQ ID NO:6, or a fragment thereof that binds to TRAF2 and either inhibits or increases the activity of NF- κ B.

21 (Previously Presented). A method for producing a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF- κ B, comprising:

growing transformed host cells in accordance with claim 16 under conditions for the expression of an expression product from said cells;

effecting post-translational modification of said expression product as necessary for obtaining said polypeptide; and

isolating said polypeptide.

22 (Currently Amended). An isolated molecule comprising an antibody, active fragment of the antibody, or derivative thereof, specific for a polypeptide according to claim 69.

23-29 (Cancelled)

30 (Currently Amended). A method for isolating and identifying a polypeptide capable of binding directly to human TRAF2, comprising applying the yeast two-hybrid procedure in which a sequence encoding said TRAF2 is carried by one hybrid vector and a sequence from a cDNA or genomic DNA library is carried by the second hybrid vector, the vectors then being used to transform yeast host cells and the positive transformed cells being isolated, followed by extraction of the extracting said second hybrid vector to obtain a sequence encoding a protein and identifying the sequence of the polypeptide encoded by said second hybrid vector, which polypeptide binds to said TRAF2.

31-42 (Cancelled)

43 (Previously Presented). A method for screening of a ligand capable of binding a polypeptide according to claim 69 comprising contacting an affinity chromatography matrix to which said polypeptide is attached with a cell extract whereby the ligand is bound to said matrix, and eluting, isolating and analyzing said ligand.

44 (Previously Presented). A method for screening of a DNA sequence coding for a ligand capable of binding to a polypeptide according to claim 69 comprising applying the yeast two-hybrid procedure in which a sequence encoding said polypeptide is carried by one hybrid vector and sequences from a cDNA or genomic DNA library are carried by the second hybrid vector, transforming yeast host cells with said vectors, isolating the positively transformed cells, and extracting said second hybrid vector to obtain a sequence encoding said ligand.

45 (Currently Amended). A method for identifying and producing a ligand capable of either inhibiting or increasing the cellular activity which is changed or mediated by TRAF2 comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least the portion of human TRAF2 having the amino acid residues 222-501 of TRAF2SEQ ID NO:23;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by the screening of (a) to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

46 (Previously Presented). A method for identifying and producing a ligand capable of either inhibiting or increasing the cellular activity which is changed or mediated by a polypeptide according to claim 53, comprising:

a) screening for a ligand capable of binding to said polypeptide;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by said screening to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

47 (Currently Amended). A method for identifying and producing a ligand molecule capable of ~~either inhibiting or increasing the cellular activity which is changed or mediated by binding to NIK~~, comprising:

- a) screening for a ligand molecule capable of binding to the NIK sequence of SEQ ID NO:7;
- b) identifying and characterizing a ligandmolecule, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by said screening step to be capable of said binding; and
- c) producing said ligand molecule in substantially isolated and purified form.

48 (Cancelled)

49 (Currently Amended). A method for identifying and producing a molecule capable of ~~directly or indirectly either inhibiting or increasing the cellular activity which is changed or mediated by binding to a polypeptide according to claim 69 comprising:~~

- a) screening for a molecule capable of ~~directly or indirectly either inhibiting or increasing the cellular activity which is changed or mediated by binding to a polypeptide according to claim 69;~~
- b) identifying and characterizing said molecule; and
- c) producing said molecule in substantially isolated and purified form.

50 (Currently Amended). An isolated molecule comprising an antibody, active fragment of the antibody, or

derivative thereof, specific for a polypeptide according to claim 53.

51-52 (Cancelled)

53 (Currently Amended). A An isolated polypeptide in accordance with claim 69, wherein said polypeptide of (a) is the polypeptide encoded by the nucleotide sequence of SEQ ID NO:6.

54 (Currently Amended). A DNA molecule comprising an isolated DNA sequence encoding a polypeptide in accordance with claim 69 or consisting of a recombinant vector comprising said DNA sequence.

55 (Currently Amended). A DNA sequence encoding a polypeptide in accordance with claim 69, molecule in accordance with claim 54, wherein said DNA sequence is selected from the group consisting of:

(i) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:1;

(ii) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:6;

(iii) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:4;

(iv) a DNA sequence consisting of a fragment of a sequence of (i)-(iii) which encodes a polypeptide that binds

to TRAF2 and either inhibits or increases the activity of NF- κ B;

(v) a DNA sequence capable of hybridization to a sequence of (i)-(iv) under moderately stringent conditions and which encodes a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF- κ B; and

(vi) any DNA sequence other than those defined in (i)-(v) which encodes a polypeptide in accordance with claim 6954.

56 (Currently Amended). A DNA sequence molecule in accordance with claim 55, comprising wherein said DNA sequence comprises the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:4.

57 (Currently Amended). A DNA sequence molecule in accordance with claim 55, comprising wherein said DNA sequence comprises the nucleotide sequence of SEQ ID NO:3.

58 (Currently Amended). A DNA sequence molecule in accordance with claim 55, comprising wherein said DNA sequence comprises a DNA sequence encoding the polypeptide encoded by the DNA sequence of SEQ ID NO:6 (protein NIK of SEQ ID NO:7)).

59 (Currently Amended). A DNA molecule in accordance with claim 54, wherein said DNA sequence encoding

(1) a polypeptide ~~in accordance with claim~~

53wherein said polypeptide of (a) is the polypeptide encoded
by the nucleotide sequence of SEQ ID NO:1, or

(2) a polypeptide that is encoded by a DNA sequence
capable of binding to a DNA sequence encoding the sequence of

(1) under moderately stringent conditions, which polypeptide
binds to TRAF2 and either inhibits or increases the activity of
NF- κ B.

60 (Previously Presented). An anti-sense
oligonucleotide consisting of a sequence complementary to at
least a portion of the mRNA encoding a TRAF2-binding
polypeptide comprising the amino acid sequence of SEQ ID
NO:2, an amino acid sequence encoded by the nucleotide
sequence of SEQ ID NO:3, or the amino acid sequence of SEQ
ID NO:5, said anti-sense oligonucleotide being capable of
effectively blocking the translation of said mRNA.

61 (Cancelled)

62 (Previously Presented). An isolated polypeptide
comprising the amino acid sequence set forth as SEQ ID NO:7 or
an analog thereof which differs from the sequence of SEQ ID
NO:7 by a substitution, deletion or insertion of a single amino
acid, which analog binds to TRAF2 and either inhibits or
increases the activity of NF- κ B.

63 (Currently Amended). A DNA molecule comprising an isolated DNA sequence encoding a polypeptide in accordance with claim 62 or consisting of a recombinant vector comprising said DNA sequence.

64 (Currently Amended). A method for identifying and producing a ligand molecule capable of either inhibiting or increasing the cellular activity which is changed or mediated by binding to a polypeptide according to claim 62, comprising:

a) screening for a ligand molecule capable of binding to said polypeptide;

b) identifying and characterizing a ligand molecule, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by said screening to be capable of said binding; and

c) producing said ligand molecule in substantially isolated and purified form.

65 (Currently Amended). A DNA molecule comprising an isolated DNA sequence encoding a polypeptide in accordance with claim 53 or consisting of a recombinant vector comprising said DNA sequence.

66 (Previously Presented). A vector comprising a DNA sequence according to claim 65.

67 (Previously Presented). Transformed eukaryotic or prokaryotic host cells containing a vector according to claim 65.

68 (Previously Presented). A method for producing a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF- κ B, comprising:

growing transformed host cells in accordance with claim 67 under conditions for the expression of an expression product from said cells;

effecting post-translational modification of said expression product as necessary for obtaining said polypeptide; and

isolating said polypeptide.

69 (Currently Amended). A isolated polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF- κ B, said polypeptide ~~comprising~~:

a) comprising the amino acid sequence of SEQ ID NO:2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO:6, or the amino acid sequence of SEQ ID NO:5;

b) comprising an amino acid sequence of an analog of a), having no more than ten changes in the amino acid sequence of a), each said change being a substitution, deletion or insertion of an amino acid, which analog binds

to TRAF2 and either inhibits or increases the activity of NF- κ B;

c) consisting of an amino acid sequence of a fragment of a), which fragment binds to TRAF2 and either inhibits or increases the activity of NF- κ B; or

d) comprising a derivative of a), b) or c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative binds to TRAF2 and either inhibits or increases the activity of NF- κ B.

70 (Currently Amended). A An isolated polypeptide in accordance with claim 62, wherein said analog is one which differs from the sequence of SEQ ID NO:7 by a single conservative substitution, said conservative substitution being one of the following:

Appln. No. 09/155,676
Amdt. dated December 14, 2005
Reply to Office action of June 14, 2005

<u>Original Residue</u>	<u>Conservative Substitution</u>
Ala	Gly; Ser
Arg	Lys
Asn	Gln; His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Ala; Pro
His	Asn; Gln
Ile	Leu; Val
Leu	Ile; Val
Lys	Arg; Gln; Glu
Met	Leu; Tyr; Ile
Phe	Met; Leu; Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp; Phe
Val	Ile; Leu;

or said conservative substitution being an exchange within
one of the following five groups:

1. Small aliphatic, nonpolar or slightly polar residues: Ala, Ser, Thr, Pro, Gly;
2. Polar negatively charged residues and their amides: Asp, Asn, Glu, Gln;
3. Polar, positively charged residues: His, Arg, Lys;
4. Large aliphatic nonpolar residues: Met, Leu, Ile, Val, Cys; and
5. Large aromatic residues: Phe, Tyr, Trp.

71 (Currently Amended). A-An isolated polypeptide in accordance with claim 70, wherein said single conservative substitution is between an alanine and a proline residue.

72 (Cancelled)

73 (Currently Amended). A-An isolated polypeptide in accordance with claim 69, wherein said analog of b) is one having no more than five of said changes in the amino acid sequence of a).

74 (Currently Amended). A-An isolated polypeptide in accordance with claim 69, wherein said analog of b) is one having no more than three of said changes in the amino acid sequence of a).

75 (Currently Amended). A-An isolated polypeptide in accordance with claim 69, wherein said analog of b) is

one having no more than one of said changes in the amino acid sequence of a).

76 (Cancelled)

77 (Currently Amended). A DNA molecule comprising
an isolated DNA sequence encoding a polypeptide in
accordance with ~~elam-claim 73~~ or consisting of a recombinant
vector comprising said DNA sequence.

78 (Currently Amended). A DNA molecule comprising
an isolated DNA sequence encoding a polypeptide in
accordance with ~~elam-claim 74~~ or consisting of a recombinant
vector comprising said DNA sequence.

79 (Currently Amended). A DNA molecule comprising
an isolated DNA sequence encoding a polypeptide in
accordance with ~~elam-claim 75~~ or consisting of a recombinant
vector comprising said DNA sequence.

Appln. No. 09/155,676
Amdt. dated December 14, 2005
Reply to Office action of June 14, 2005

Amendments to the Sequence Listing:

Please enter the attached Sequence Listing,
numbered as pages 1-54.

Please substitute the attached Sequence Listing
section for the Sequence Listing filed April 4, 2005.

A new computer-readable form is also attached.